DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

CBER-01-010

JAN 23 2001

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Richard J. Manassa
President
Allergy Laboratories of Ohio, Inc.
623 E. 11th Avenue
Columbus, OH 43211

Dear Mr. Manassa:

The Food and Drug Administration (FDA) conducted an inspection September 19 through September 26, 2000, of Allergy Laboratories of Ohio, Inc., located at 623 E. 11th Avenue, Columbus, Ohio. During the inspection, the FDA investigator documented violations of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) and deviations from the applicable standards and requirements of Title 21, Code of Federal Regulations (CFR), Parts 210-211 and 600-680 as follows:

1. Failure to establish testing programs designed to assess the stability characteristics of drug products [21 CFR 211.166(a)], in that:

   a. Orchard Grass Pollen extract and Sweet Vernal Grass Pollen extract, which are labeled with three year expiry dates, have only 24 and 18 months stability data, respectively.

   b. stability data has not been generated for standardized Mite extract since October, 1988.

   c. testing intervals were missed on numerous occasions for Meadow Fescue Grass Pollen, Kentucky Blue Grass Pollen, Perennial Ryegrass Pollen, Timothy Grass Pollen, and others.

d. stability testing of the above grass pollens was limited to potency. Sterility or container/closure integrity testing and preservative analysis were not performed.

2. Failure to establish the effectiveness or verify the suitability of all testing methods under actual conditions of use [21 CFR 211.194(a)], in that the suitability of the test methods for Glycerin Titration, Isoelectric Focusing, Radial Immune Diffusion (RID), and Phenol by high pressure liquid chromatography (HPLC) have not been verified under actual conditions of use. The effectiveness of the test method Phenol by HPLC has not been established.

3. Failure to conduct a thorough investigation of any unexplained discrepancy or failure of a batch to meet its specifications [21 CFR 211.192], in that an investigation was not conducted to determine the origin and nature of precipitates that were found in eight batches of extracts.

4. Failure to establish and document the accuracy, sensitivity, specificity and reproducibility of test methods [21 CFR 211.165(e)], in that bacteriostasis/fungistasis testing has not been performed for sterility testing procedures.

5. Failure to include the establishment of scientifically sound and appropriate specifications, standards, sampling plans and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling and drug products conform to appropriate standards of identity, strength, quality and purity [21 CFR 211.160(b)], in that in-house standards used for glycerin, phenol, and RID analyses have not been qualified.

6. Failure to establish written procedures for a review of records associated with a batch [21 CFR 211.180(e)], in that annual reviews of records are not performed.

7. Failure to visually examine reserve samples from representative lots or batches for deterioration at least once a year [21 CFR 211.170(b)].

During the inspection, the investigator documented at least seven lots of extracts that were recalled after errors were discovered in either the concentration calculations or expiration dates. Although the lots were recalled, please be advised that Allergy Laboratories of Ohio must promptly notify the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research (CBER) of errors or accidents in the manufacture of products that may affect the safety, purity, or potency of any products [21 CFR 600.14(a)].

We acknowledge receipt of your response dated October 26, 2000, which addresses the inspectional observations on the Form FDA 483 issued at the close of the inspection. Corrective actions addressed in your letter may be referenced in your response to this

letter, as appropriate; however, your response did not provide sufficient detail to fully asses the adequacy of the corrective actions. Our evaluation of your response follows, and is numbered to correspond to the items listed on the Form FDA 483:

Item 2A & B:

The last paragraph of the response includes a statement regarding re-filtration of extracts that exhibit precipitates. A validation study should be performed to ensure additional filtration does not affect the potency or stability for standardized products. In addition, the number of times a product can be refiltered needs to be defined and supported by data. The protocol and study results should be submitted under Changes to an approved application [21 CFR 601.12(b)].

Item 10:

Manual verification of calculations and inventory tracking with the existing computer software that has been found to be problematic is not an adequate reason for lack of validation. Existing computer software should be validated or replaced.

Item 15:

Personnel monitoring specifications should be based on process capability and historical data.

Item 16:

Please describe the method to be used to depyrogenate vials and stoppers.

The above violations are not intended to be an all-inclusive list of deficiencies at your establishment. It is your responsibility as President to assure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the Form FDA 483 issued at the close out of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

You should take prompt measures to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Such actions include, but are not limited to, license suspension and/or revocation, seizure and/or injunction.

Please notify this office within 15 days of receipt of this letter, of the specific steps you will take to comply with our request. If corrective action cannot be completed within 15

working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to the Food and Drug Administration, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Suite 200 N, Rockville, Maryland 20852-1448, Attention: Division of Case Management, HFM-610. If you have any questions regarding this letter, please contact Janet Claggett at (301) 827-6201.

Sincerely,

Deborah D. Ralston
Director
Office of Regional Operations